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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,272	12/15/2003	Yu-Fang Hu	MR929-944	1490

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1615

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/734,272	Applicant(s) HU ET AL.	
	Examiner Gollamudi S. Kishore, Ph.D	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims included in the prosecution are 1-30.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The distinction between lecithin and phosphatidylcholine in claim 1 is unclear. Another name for phosphatidylcholine is lecithin.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1- 24, 26-28 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Slater (6,355,268).

Slater discloses a process of preparation of liposomes. The process involves mixing soy phosphatidylcholine, cholesterol and PEG-DSPE in a mole ratio of 56. 4: 38.3: 5.3 in ethanol at 65 degrees and mixing this mixture with an ammonium sulfate solution at 65 degrees. The mixture is subjected to an extrusion process through an extruder. The ammonium sulfate and ethanol are removed from the external bulk

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aqueous phase prior to loading the active agent by diafiltration, which could be interpreted as a dialysis process. The active agent, Topotecan is dissolved in 40 ml of 10 % sucrose solution and then remotely loaded. (abstract, col. 7, line 20 through col. 9, line 23 and Example 1). The amounts of individual components in Slater fall within the ranges instantly claimed.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slater (6,355,268) by itself or in combination with Zalipsky (6,051,251).

Slater discloses a process of preparation of liposomes. The process involves mixing soy phosphatidylcholine, cholesterol and PEG-DSPE in a mole ratio of 56.4: 38.3: 5.3 in ethanol at 65 degrees and mixing this mixture with an ammonium sulfate solution at 65 degrees. The mixture is subjected to an extrusion process through an extruder. The ammonium sulfate and ethanol are removed from the external bulk aqueous phase prior to loading the active agent. The active agent, Topotecan is dissolved in 40 ml of 10 % sucrose solution and then remotely loaded. The method of Slater differs from instant method in that, the ammonium sulfate and ethanol are

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removed by diafiltration and not by dialysis process (abstract, col. 7, line 20 through col. 9, line 23 and Example 1). One could however, interpret diafiltration as a dialysis process. Since the goal is to remove ammonium sulfate and ethanol from the liposomal mixture, it would have been obvious to one of ordinary skill in the art to use art known process of dialysis, which removes salts with a reasonable expectation of success. One of ordinary skill in the art would be motivated to use this process since the reference of Zalipsky shows the removal of ammonium sulfate from the external medium by dialysis and also equates dialysis and diafiltration for the removal of small molecular weight compounds such as drugs (Example 1 and col. 8, lines 12-16). Although Slater does not disclose claimed ranges for the individual components, since both instant invention and Slater are involved in the process of preparation of liposomes loaded with the active agents, it is deemed obvious to one of ordinary skill in the art to manipulate the amounts of the phospholipids and ethanol to obtain the best possible results. Slater does not disclose the active agent to be doxorubicin. However, since the principle of loading the active agent is the same, one of ordinary skill in the art would be able to load any active agent in the method of Slater with a reasonable expectation of success. Although Slater does not teach lyophilization of liposomes, since this step is routinely practiced in the art of liposomes, one of ordinary skill in the art would be motivated to lyophilize the liposomes with a reasonable expectation of success.

7. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Slater (6,355,268) by itself or in combination with Zalipsky (6,051,251) as set forth above, further in view of Papahadjopoulos (6,426,086).

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The teachings of Slater and Zalipsky have been discussed above. What is lacking in Slater and Zalipsky is the lyophilization of the liposomes.

Papahadjopoulos teaches that liposomes can be lyophilized and the lyophilized product can be combined with a sterile aqueous solution prior to administration (col. 19, lines 33-36). To include a step of lyophilization in the method of Slater would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since the reference of Papahadjopoulos shows that it is a commonly used step in the method of preparation of liposomes and administration of said liposomes.

8. Claims 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slater (6,355,268) by itself or in combination with Zalipsky (6,051,251) as set forth above, further in view of Barenholz (5,316,771).


The teachings of Slater and Zalipsky have been discussed above. What is lacking in Slater and Zalipsky is the teaching of doxorubicin as the active agent. The use of doxorubicin as the active agent in the liposomes of Slater would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since the reference of Barenholz shows the loading of doxorubicin in liposomes containing ammonium sulfate (fig. 3, examples and claims).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK